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10/790,640	03/01/2004	Michael D. West	75802.026014	9766

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/790,640	WEST ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8,10-12,14-16,21-25,27-36 and 106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8,10-12,14-16,21-25,27-36 and 106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply dated 12/07/2009 has been received. Claims 21-22,25, and 27 are amended. Claims 2,9,13,17-20,26 and 37-105 have been cancelled. Claims 1,3-8,10-12,14-16,21-25,27-36 and 106 are pending and under consideration in the instant office action.

The instant application is a continuation of USSN 09/527,026, now abandoned.

Claim Objections

Claim 16 remains objected to because of the following informalities: Claim 16 depends from a cancelled claim. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1,3-8,10-12,14-16,21-24,29-36 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 87-92,94-117 of copending Application No. 11/079,930. Although the conflicting claims are not identical, they are not

patentably distinct from each other because while the claims of '930 are not specifically drawn to mammals, the instant claimed methods utilizing reprogramming of somatic cell nuclei by nuclear transfer were notably used in mammalian species. Thus, the generic claimed "cell" in '930 renders obvious the instant claimed mammalian cell..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant previously requested that this rejection be held in abeyance until otherwise allowable subject matter is identified, at which time, the filing of a TD will be considered.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following rejections under 35 US 112 1st paragraph are maintained separately for the sake of clarity. The remaining grounds of rejection are essentially the same in each rejection.

1) Claims 1,3-8,10-12,14-16 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method using *fibroblast* donor cells, does not reasonably provide enablement for the claimed method using any donor cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method of nuclear transfer using a near senescent or senescent donor cell of any type to form a blastocyst, isolation of a whole or part of the developing blastocyst, formation

of a teratoma with said blastocyst whole or part, and isolation of a cell from the teratoma to obtain a cell with increased remaining populations compared to the donor.

The claims were previously deemed enabled for use of fetal fibroblasts as a donor cell. The enabled scope has been expanded to include any fibroblast cell, including fetal or adult fibroblasts as fibroblasts have an increased lifespan over other adult cells and their use in the instant invention is exemplified in Example 3, which demonstrates adult dermal fibroblasts have an increased lifespan in culture.

The specification teaches carrying out the claimed method using a fetal fibroblast wherein the resulting cell has increased telomere length. The increased telomere length was an unexpected and novel finding as the earlier Dolly cloning using mammary epithelial cells was found to result in cell with shortened telomeres. Post-filing, Lanza reported the lengthening of telomeres in cells resulting from nuclear transfer in **Science** (2000, 288:665-669). Lanza explains that the apparent discrepancy in the length of the telomeres in cloned cells may be due to cell type used (see page 668, col. 3). Denning (2001, of record) teaches primary cells have limited proliferation capacity (Denning, page 222, col. 1, lines 5-8). In a study of sheep and goat primary somatic cells, Denning found that *of primary somatic cells, fibroblasts were the only cells* that either grew at all from the primary cell source or has sufficient population doublings for the selection required in targeted gene transfer. Sheep primary cell cultures primarily were composed of fibroblasts after the third passage or about 12 doublings (Denning, page 224, col. 2, lines 11-13). In a similar analysis of pig primary cultures, fibroblasts, as in the sheep study, became the predominant cell-type after three passages (Denning, page 224, col. 2, parag. 4 line 4 to page 225, col. 1, line 8).

Applicant argues that pages 36-37 of the specification shows five adult derived cells gave rise to blastocysts by nuclear transfer (see pages 10-11 of Applicant's Remarks). However, the five cells were all of the same type-fibroblasts. Thus, the example fails to enable any type of adult-derived cell other than

fibroblast. Accordingly, the art at the time of filing supported that the lifespan of adult-derived fibroblasts was greater than other adult-derived somatic cells and as such, only fibroblasts were successful in achieving the invention as claimed.

Applicant also argues that the Ulaner reference that was relied upon in the rejection fails to mention the term "fibroblast". In response, the Ulaner reference is no longer applicable to the rejection as it was relied upon in support of limiting the claims to fetal cells, which is no longer required. In this respect, Applicant's arguments are persuasive. The rejection, now limiting the donor cells to fibroblasts in general, not just fetal fibroblasts, relies on the demonstration in the art that fibroblasts differ from other cell types used as donors in nuclear transfer in that they have an increased life span prior to nuclear transfer, affecting their ability to be genetically manipulated and used in SCNT.

Applicant also argues that it would not require undue effort for one of skill in the art to identify other operative embodiments of the claim (pages 13-14 of Remarks). In response, the specification teaches only use of adult and fetal fibroblasts in carrying out the claimed method and fails to demonstrate a single other donor cell that is useful in the claimed invention. Given the demonstration in the art that fibroblasts appear to be exceptional in their ability to be cultured in vitro to near senescence prior to nuclear transfer while other somatic cell types fail to have this replicative capacity, the specification fails to support that any other donor cell type would be operable as claimed. Applicant is not required to demonstrate each and every somatic cell type encompassed by the claims would be operable. However, in light of the art demonstrating a clear delineation and difference between most somatic cell types and fibroblasts, the specification should show that cell types other than fibroblasts could be used in the method as claimed.

2) Claims 7,14,21-25,27-36 and 106 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods for the claimed method using fibroblasts as donors does not reasonably provide enablement for the claimed method using any donor

cell other than a fibroblast. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The rejection is maintained in part. As set forth in the previous office action dated 06/05/2009, the art held that cells other than fibroblasts that are maintained in culture prior to use in NT are not effectively reprogrammed. Adult somatic cells have a very limited lifespan and their culture to a near senescent state prior precluded their use as donors for nuclear transfer. The specification teaches use of senescent or near-senescent adult and fetal fibroblast cells, i.e. they have completed 90-95% of their lifespan with less than 2-3 population doublings remaining, in nuclear transfer. The specification does not teach passage of any cell other than fibroblasts, as claimed, to a near-senescent state prior to NT.

Applicant comments that it is not clear why claims other than 7 and 14 are included in this rejection. The other claims are included because claim 21 requires genetic manipulation, and, as set forth in the rejection of record, genetic manipulations requiring homologous recombination, as well as any nuclear transfer protocol requiring culture to near senescence, is only enabled for fibroblasts.

Applicant argues that the claims do not require that the cell be near senescent at the time of genetic manipulation, i.e. the cell could have been genetically manipulated at some other time point (see page 14, paragraph 2 of Remarks). In response, the claims encompass homologous recombination in senescent cells as well as non-senescent cells not having enough lifespan remaining for appropriate nuclear reprogramming and nuclear transfer. Applicant views the use of senescent cells in carrying out homologous recombination prior to nuclear transfer as an inoperable embodiment. This is not the case as claim 7 specifically recites that a native gene is disrupted and one of skill in the art would readily envision homologous recombination (i.e. gene-targeting) as a means of gene disruption.

Applicant also argues that one could readily test other cell types in carrying out the claimed method and the claims should not be limited to fibroblasts, which are the only cells used in the

specification (page 15 of Remarks). In response, while one could readily test various cell types as nuclear donors, the art holds that only a single cell type, fibroblasts, is competent in being passaged in vitro to near-senescence, whether passaged to attain homologous recombination or not. The specification only demonstrates success using that single cell type. Thus, there is no evidence of record indicating that nay cell type other than fibroblasts can be cultured to near senescence prior to use in NT.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 25 remains confusing and unclear. Applicant has amended the claim to read "a primary mammalian cell that has been genetically altered". However, there is not baseline for determining the alteration. The alteration could be a result of DNA methylation, changes in DNA conformation, insertions, deletions, mismatches. Some of these require active, intentional genomic alterations after isolation of the primary cell. Others, are descriptive of any cell prior to isolation. Thus, it is not clear what is encompassed by the claim. Applicant has failed to address this aspect of the rejection.

The remaining aspects of the rejection are withdrawn in light of Applicant's amendments to the claims and remarks.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing

date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632